THE EFFECTS OF SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRI) ON AUDITORY MEASURES IN CLINICALLY DEPRESSED SUBJECTS

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The purpose of this study was to investigate the relationship between selective serotonin reuptake inhibitor (SSRI) medication on auditory skills in clinically depressed subjects. Experimental subjects prescribed an SSRI were tested in a medicated and an unmedicated condition, and the test results were compared. Furthermore, the experimental group was compared with a control group consisting of normal subjects. Test measures included pure tone audiometry, tympanometry, acoustic reflex thresholds, and auditory electrophysiologic measures such as auditory brainstem and auditory late responses. An assessment scale for depression (Beck Depression Inventory-II) was also used. Results indicated statistically significant differences for the BDI-II between the control and experimental groups for both conditions. Electrophysiologic measures indicated a significantly shorter latency for auditory late potential P1 at 55 dBnSL, and a significantly larger amplitude at 45 dBnSL for the N1/P2 component for the unmedicated group. Although the other measures showed trends, they did not reach significance.

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CHAPTER 1

INTRODUCTION

Neurotransmitters are chemicals released by the axon of a neuron into a space located between the axon and adjacent neuron called the synaptic cleft. These chemicals either bind to the adjacent neuron to provide an excitatory or inhibitory response, or get oxidized and taken up by the presynaptic cell for resynthesis of that chemical. Serotonin (5-hydroxytryptamine, 5-HT), a biogenic amine, is a classical neurotransmitter, widely dispersed in the central nervous system as well as in the peripheral nervous system. Presynaptic and postsynaptic actions of 5-HT occurring in the peripheral, enteric (intestine), and central nervous systems include hyperpolarization, depolarization, and potentiation of norepinephrine and dopamine release, potentiation and inhibition of acetylcholine release, and regulation of vascular tone (Vandermalen, 1985). Serotonin is both an excitatory and inhibitory neurotransmitter used by the auditory system to facilitate sensory information processing (Jacobs & Fornal, 1993). The various actions of 5-HT in the brain and periphery can manifest as disorders when disrupted. They can be expressed as affective disorders or disorders disruptive to a particular sensory system. Some disorders related to serotonin include depression, obsessive-compulsive disorders, hyperacusis, migraine headaches, and other psychiatric disorders (Hegerl et al., 1998).

Research conducted by Thompson et al. (1994) found that many 5-HT receptor subtypes were located in the auditory system including the cochlear nucleus as well as the

inferior colliculus of the brainstem. They concluded that since the auditory system is innervated by many serotonergic fibers and terminal endings, 5-HT may modulate central auditory processing by tonic inhibition of acoustic pathways. Patients with migraines who also have symptoms of hyperacusis were described in their research as evidence of 5-HT in the auditory system, which functions as a regulator of primary sensory pathways. Many patients with these disorders also exhibit a low concentration of serotonin in plasma and also platelets of the blood (Sarrias et al., 1987). Treatment of serotonin disorders by use of selective serotonin reuptake inhibitors (SSRIs) is common in the United States as well as in other countries. This research addressed the effects of SSRI on auditory measures in patients with unipolar depression.

A case study exhibiting the auditory effects of serotonin was documented by Gopal et al. (2000). A female subject with clinical symptoms of hyperacusis, difficulty understanding speech, withdrawn depression, lethargy, as well as hypersensitivity to touch, pressure and light was evaluated in both an unmedicated and medicated condition. The medicated condition consisted of treatment by an SSRI that supposedly blocks the mechanism for reuptake of serotonin back into the presynaptic neuron, and therefore allows a higher concentration of serotonin to accumulate in the postsynaptic cleft. This patient was evaluated over the course of 18 months using auditory processing tests, evoked potentials, impedance testing, otoacoustic emissions, and uncomfortable loudness measures. Significant differences were observed between medicated and unmedicated conditions for transient evoked otoacoustic emissions, uncomfortable loudness levels, and auditory processing skills as reflected in the SCAN-A (A screening test for auditory processing in adolescence and adults.) test scores. Further research relating SSRI and

auditory processing abilities of clinically depressed patients was recommended for a larger sample of patients with similar clinical symptoms.

Carney (2001) further investigated the role of SSRIs on peripheral and lower brainstem auditory processing. Clinically depressed subjects taking SSRI (medicated condition) were compared with depressed subjects not taking any SSRI (unmedicated condition). A control group of subjects that neither exhibited an affective disorder nor had taken any SSRI medication was also used in the study. Tests included in Carney's research were uncomfortable loudness measures (UCL), otoacoustic emissions with contralateral masking, masking level difference (MLD), acoustic reflexes, intensity resolution, and temporal integration. Although statistical significance was not reached when comparing these three groups, a general trend toward lower UCL, and a smaller dynamic range was observed in the unmedicated group when compared to the medicated and control groups. Acoustic reflex thresholds did not show significant differences between the three groups. The unmedicated group also showed a smaller difference limen for intensity as compared with the control and medicated groups. Masking level difference showed a trend for a smaller release from masking in unmedicated subjects as compared to control and medicated subjects. The Beck Depression Inventory-II, however, showed statistical significant difference between both experimental groups and the control group. It was recommended that comparison be made between the test results obtained during medicated and unmedicated conditions for the same set of subjects.

In a related study, Bishop (2001) investigated the role of SSRI on the central auditory system. Auditory brainstem response (ABR), auditory late response (ALR),

and auditory tests using speech stimuli were compared between control, unmedicated, and medicated subjects. The loudness dependence of ABR for peak V is described by Hegerl et al., (1993) as an increase in amplitude with intensity increase, showed significant differences between unmedicated subjects and control subjects as did the –20 message to competing ratio (MCR) condition on the Synthetic Sentence Identification test (SSI). Other electrophysiology measures such as absolute latency for peak V, the amplitude increase for the N1/P2 component of the ALR, and the right ear scores for the -20 MCR condition of the SSI were not significant but showed a trend between the unmedicated and control groups. It was suggested that intra-subject comparison and a larger sample size be used for further studies.

Goals of the Study

This study investigated the role of SSRI medication on auditory measures using intra-subject comparison. Experimental subjects who were clinically depressed were tested in a medicated and unmedicated condition. This group consisted of subjects diagnosed by a physician as clinically depressed according to the criteria as set forth by the referring physician and the DSM IV (Diagnostic and Statistics Manual for Mental Disorders-IV), then treated with one of the five SSRIs that included Prozac, Zoloft, Celexa, Paxil, or Luvox. A control group consisting of normal subjects was also evaluated that neither had a history of depression nor was taking any SSRI medication. Tests used in this study were otoscopy, tympanometry, pure-tone thresholds, acoustic reflexes, amplitude resolution, auditory brainstem response (ABR), and auditory late response (ALR). These tests measure the integrity of the auditory system and can reveal the function of the auditory system at several different levels. The Beck Depression

Inventory-II was used to quantify the depressive symptoms of each patient and to assess correlation with the other tests used.

Specific questions of this study include:

1) Were there significant differences in acoustic reflex thresholds and amplitude resolution test results between medicated and unmedicated conditions of the experimental group?
2) Were there significant latency and amplitude differences between ALR waves P1 and N1 and ABR peak V between medicated and unmedicated conditions of the experimental group?
3) Were there significant differences in any of the test measures between the control group and experimental group?

CHAPTER 2

REVIEW OF LITERATURE

Prelude

Each auditory measure used in this research is related to some aspect of serotonin in the brain. Research on depression and serotonin is extensive, however, the specific effects they have on the auditory system is more obscure. The relationship between serotonin and how it functions to regulate auditory information will be described by relevant research as well as the effects a disruption of serotonin may have on auditory processing.

The tests selected in this research measure auditory function and will be described from peripheral to central. Tests reviewed for this research are acoustic reflex thresholds, amplitude resolution, auditory brainstem response, and auditory late response. The Beck Depression Inventory-II also included in this study is a scale which measures depression and is relevant is assessing the presence of depression in individuals in the experimental group. The tests selected for this research are widely available and are used frequently in research and clinical settings.

Serotonin

Serotonin (5-hydroxytryptamine; 5-HT) is a neurotransmitter found in the vertebrate central nervous system and is categorized as a biogenic amine synthesized in the indole nucleus and therefore further classified as an indolemine (Vandermaelen, 1985). Neurotransmitters function as messengers that facilitate excitatory or inhibitory responses by acting on postsynaptic receptors. Currently up to seven receptor classes have been identified and within these classes, receptor subtype classes have been recognized as well (Martin & Humphrey, 1994). Uphouse (1997) suggested the importance of multiple receptor subtypes might provide advantage to certain species by allowing flexibility, which enables the nervous system to receive and integrate information more efficiently than would be possible with only one receptor subtype. The various actions of 5-HT such as regulation of sleep-wake-arousal cycle (Jacobs & Fornal, 1999; Imeri et al., 2000), motor output (Jacobs & Fornal, 1993), inhibition of sensory information (Stutzmann et al., 1998), regulation of cerebral blood flow (Vandermaelen, 1985), and regulation of temperature (Vandermaelen, 1985; Imeri et al., 2000) are examples of the influence this neurotransmitter has on various functions. Most all of the 5-HT cell bodies occur in the raphe nuclei of the brainstem or near the midline and were associated with functions such as controlling trunk and proximal limb muscles (Jacobs & Fornal, 1999), though 5-HT receptors also occur in areas of the brain which regulate mood and anxiety (Martin & Humphrey, 1994). Serotonergic neurons innervate

all levels of the central nervous system (Vandermaelen, 1985) and there is evidence that 5-HT is involved in similar excitatory and inhibitory roles in the auditory system.

Serotonin in the Auditory System

Thompson et al., (1994) described in three mammalian species the presence and relative density of 5-HT in the brainstem auditory nuclei. Thompson and colleagues noted that the presence of serotonin in these structures might play a modulatory role in the primary sensory pathways such as tonic inhibition of the acoustic reflex. It was further added that 5-HT should be considered when evaluating auditory pathophysiology. Fitzgerald and Sanes (1999) observed direct evidence of 5-HT innervation of the auditory nuclei specifically the lateral superior olive (LSO), which is the primary site of binaural convergence of the afferent auditory fibers. They also concluded that 5-HT may play a modulatory role in the auditory system.

Evidence of serotonin in the cortical auditory system is found in the augmenting reducing effect of the N1/P2 component of the ALR. The ALR is generated by the primary auditory cortex (Pantev et al., 1990) or Broadman's areas 41 and 42 (Brown et al., 1979). This area is greatly innervated by serotonergic neurons and is therefore rich in serotonin synthesis like most sensory areas (Brown et al., 1979). The auditory cortex has the highest synthesis rate and cortical concentration of serotonin out of all the sensory processing centers of the brain (Azmitia & Gannon, 1986; Lewis et al., 1986). Patients who show lower levels of serotonin have larger amplitudes of the N1/P2 component, which are pronounced at higher intensities (Hegerl et al., 1998; Juckel et al., 1999).

Several studies have shown 5-HT to be a factor in the manifestation of auditory disorders in humans, such as hyperacusis (Marriage & Barnes, 1995; Gopal et al., 2000), tinnitus (Simpson & Davies, 2000), and auditory processing disorders (Gopal et al., 2000). Patients presenting with clinical symptoms of depression also exhibit symptoms related to the auditory system.

Hyperacusis is described by Marriage and Barnes (1995) as an unusual hypersensitivity or discomfort induced by exposure to sound. They categorize hyperacusis as a separate phenomenon to recruitment, which is an abnormal loudness growth usually associated with peripheral hearing loss. Hyperacusis like tinnitus therefore cannot be measured objectively and may be under reported when it occurs concurrently with other pathologies such as tinnitus and headache. As compared with recruitment, hyperacusis occurs in patients with normal hearing. Hyperacusis is often concurrent with photophobia and tinnitus, which are often present with other disorders related to 5-HT dysfunction or dysregulation. Marriage and Barnes (1995) conclude on the basis of research and clinical evidence that the primary cause of central hyperacusis is related to 5-HT function.

Disorders Related to Serotonin

Disorders related to the serotonergic system include obesity, compulsive disorders such as alcoholism and bulimia, and depression (Lucas, 1992). The presence of major depression in the general population ranges from 4-9% affecting 10 % of men and 20 % of women at some point in their lives (Alarcon, et al. 1998). Depression is an illness that is often chronic and recurrent affecting 12% of the treated population for as long as 5

years with some people experiencing relapses up to ten years after treatment (Hirschfeld, 1994). Depression is often difficult to diagnose and treat because the course of illness can be variable (Geringer & Wool, 1994) and symptoms can be masked by physical complaints and often coexist with other medical problems (Alarcon et al., 1998).

Diagnosis of depression by primary care physicians and psychiatrists is achieved systematically using criteria set forth by the Diagnostic and Statistics Manual of Mental Disorders-IV (DSM-IV). Major depressive disorders must fit the criteria for a depressed mood or loss of interest that lasts for at least two weeks and is accompanied by at least four additional symptoms of depression. Some symptoms of depression as specified by the DSM-IV include loss of appetite, insomnia, agitation, decreased energy, feeling worthless or fatigued, and loss of interest or pleasure. Depression may also be accompanied by other disorders such as eating disorders, disorders of anxiety or panic, or depression exhibiting specific features such as psychotic episodes or seasonal patterns of onset.

Patients suffering from depression, obsessive-compulsive disorders, and other psychiatric disorders are commonly treated with serotonin reuptake inhibitors (SSRIs) (Hegerl et al., 1998; Bruder et al., 2001). SSRI medications act by blocking the reuptake mechanism for reabsorption of serotonin in the presynaptic cleft therefore allowing more accumulation of the neurotransmitter (Fuller & Wong, 1990; Pinder, 1997). SSRIs and polycyclics are two major categories of antidepressants (Geringer & Wool, 1994). However, SSRIs are more commonly prescribed because they carry fewer side effects and have a high safety profile when taken alone in an overdose situation (Geringer &

Wool, 1994) as compared to the mortality rate of 70-80% associated with overdose of polycyclic antidepressants (Alarcon et al., 1998).

It has been observed by several researchers that patients exhibiting symptoms of affective disorders also have lower levels of serotonin in the blood (Sarrias et al., 1987; Perez et al., 1998). The amine hypothesis of depression describes the underlying malfunction of this illness as related to the depletion or dysregulation of norepinephrine and/or serotonin in the brain (Geringer & Wool, 1994). This decrease in the production and possible abnormalities in the uptake by receptors are found to be closely associated with depression (Geringer & Wool, 1994). The decrease in serotonin levels can be treated and help alleviate the symptoms related to this dysfunction. SSRIs act to inhibit the reuptake of 5-HT allowing accumulation of 5-HT in the synaptic cleft of the presynaptic neuron (Fuller & Wong, 1990; Pinder, 1997).

Patients with depression who also have pathological auditory symptoms such as hyperacusis, auditory processing disorders, and tinnitus show benefit from these medications. A patient treated with an SSRI showed a greater dynamic range by elevation of the uncomfortable loudness level (UCL), reduced transient evoked otoacoustic emissions, improved auditory processing, and alleviation of hyperacusic symptoms (Gopal et al., 2000). Treatment of serotonin related disorders with SSRI medication has a direct effect on tests related to hearing and auditory processing.

Acoustic Reflex Thresholds

The acoustic reflex threshold (ART) is the contraction of the stapedius muscle located in the middle ear to sufficiently loud stimuli. Contraction of the

stapedius muscle occurs both ipsilaterally and contralaterally to acoustic stimulation. The pathway for the ipsilateral response begins in cochlea and is transmitted by the auditory nerve to the ipsilateral ventral cochlear nucleus (Thompson, 1983). The majority of these pathways pass through the medial part of the facial motor nucleus and then travel down the facial nerve, which is innervated by the stapedius muscle attached to the ossicles of the middle ear. Contralateral contraction of the stapedius is due to the decussating pathway of the medial superior olive in the brainstem, which then follows the contralateral pathway of the facial motor nucleus to the facial nerve, then innervating the stapedius muscle of the contralateral ear. (Jerger, 1970)

The acoustic reflex threshold is a widely accepted measure of auditory pathway integrity and can be incorporated into a protocol sensitive for retrocochlear pathology (Bauch et al., 1983). Patients with normal auditory function typically present with normal ARTs. Patients with facial nerve and vestibulocohlear nerve lesion often have absent reflexes as do patients with middle ear pathologies (Jerger, 1970; Marriage & Barnes, 1995; Hunter et al., 1999). Elderly patients with normal hearing show elevated acoustic reflex thresholds when elicited by a broadband stimulus (Gelfand & Piper, 1981).

Amplitude Resolution

The detection of difference in small changes in intensity of a signal is often referred to as amplitude resolution (Fastl and Schorn, 1981). Suprathreshold tests, such as discrimination between loudness of tones, are diagnostically relevant because sounds of life are generally above threshold (Fastl and Schorn, 1981). Level discrimination can

be measured with either modulated or pulsed tones. Fastl and Schorn (1981) explained that this difference in stimulus produces different results, which are related to the underlying processing mechanism. The modulated tone creates an excitation pattern along the basilar membrane that is constant and when changed by an increase in intensity will immediately be detected by the auditory centers of the brain. Pulsed tones however, involve more auditory processing because the excitation pattern of the tone must be stored then compared to the second tone. Fastl and Schorn (1981) reasoned that pulsed tones require higher centers of the auditory pathway than modulated tones.

Auditory Brainstem Response

The auditory brainstem response (ABR) measures the integrity of the auditory pathway from the VIIIth nerve to the midbrain (Moller et al. 1981, 1982). Wave I and II of the ABR is generated in the peripheral auditory system while wave III is generated by the cochlear nucleus and the trapezoid body of the brainstem while waves IV and V are generated by the superior olivary complex and the lateral lemniscus respectively (Moller et al. 1981, 1982). Auditory evoked potentials are used to measure several areas of the auditory pathway and can be grouped by latency. Latency describes the time interval from the onset of stimulus and the generation of the evoked potential waveform.

The ABR occurs within 10 ms following the onset of the stimulus. The ABR can be used to estimate hearing thresholds and assess the integrity of the auditory system (Galambos & Hecox, 1978). Many factors influence the ABR including age and gender. The ABR is also influence by neurotransmitter transmission including serotonin

(Bhargava et al., 1981). This is evident when disorders related to serotonin are studied using auditory evoked potentials.

Knott et al. (1994) showed brainstem involvement in panic disorder as an increase in amplitudes of waves III and V. Latencies however where unaffected. Nolfe et al. (1998) showed patients with obsessive-compulsive disorders to have significantly increased interpeak latencies between I-V for the right ear as compared with controls. They also showed significant in a decrease in amplitude of wave III as compared with controls.

Auditory Late Response

The auditory late response occurs between 150 & 300 ms and is generated by the primary auditory cortex (Hegerl & Juckel, 1993). Three main landmarks may be observed at these latencies; P1, N1, and P2. The amplitude stimulus intensity function or ASF slope describes an increase in amplitude as intensity increases (Hegerl & Juckel, 1993). The ASF slope is proposed to be a direct result of decreased serotonergic transmission (Hegerl & Juckel, 1993) and an increase in serotonergic activity results in a decrease in the ASF slope (Juckel et al., 1999). Hegerl and Juckel (1993) indicated serotonin as the primary neurotransmitter for this effect as this slope is greatly enhanced by reduced central serotonergic neurotransmission. This research suggests that the intensity dependence of the N1/P2 component may be a noninvasive way to diagnose low serotonin levels. Juckel et al. (1999) proposes that event related potentials such as the ALR could be used to more effectively treat patients with disorders of the serotonergic system by identifying them more efficiently and treating them more specifically.

Dierks et al., (1999) found that the intensity dependence of AEP's is not an indicator of central serotonergic activity. This was shown by manipulating the levels of central serotonergic activity indirectly, by decreasing the levels of tryptophan, which is necessary for the synthesis of serotonin. The decrease in tryptophan in the central nervous system has shown to decrease the levels of serotonin in animal and human studies using positron emission topography (PET) scans (Nishizawa et al., 1998). By decreasing the level of tryptophan and therefore serotonin synthesis. Dierks and his colleagues should have seen the same intensity dependence of N1/P2 as the research conducted by Hegerl (1993). However, they observed reduced intensity dependence as a result of low tryptophan levels. Debener et al., (2002) showed a similar result in research that compared a depletion of tryptophan group to a placebo group. They also found that depletion of tryptophan is not related to the ASF slope and therefore does not reflect central serotonergic transmission. How this relationship is directly related to low tryptophan or whether serotonin is affected at a later stage in the process is not clear.

Event related potentials are affected by disorders related serotonergic dysfunction such as migraine (Sand & Vingren, 2000), panic disorder (Knott et al., 1994), schizophrenia (Lindstrom et al., 1990), and obsessive-compulsive disorder (Nolfe et al., 1998). There is evidence that medications and their effects can be observed in event related potentials as well (Roon et al., 1999; Hegerl et al., 1992; Bruder et al., 2001). However, controversy suggests more research needs to be done in this area.

Concu et al., (1977), described effects of low 5-HT levels on latency in auditory evoked potentials in rats. The 5-HT levels of the brain were decreased by injection of p-chlorophenylalanine (PCPA), which selectively inhibits tryptophan necessary for 5-HT

synthesis. When the levels of cerebral 5-HT were reduced in the rat brain, the latencies were also markedly reduced. An increase in the levels of cerebral 5-HT showed an increase in latency. They explained that the primary function of serotonin in the brain is to inhibit responses in the afferent pathway. A decrease in cerebral 5-HT will cause the central acoustic pathway to be less inhibited and exhibiting less control over the response.

Auditory evoked potentials are an objective method for examining the auditory pathway and can give indirect information about the mechanisms that affect the integrity of that pathway. Other measures such as ARTs, pure-tone thresholds, and amplitude resolution can give information about the auditory system but they tell little about the perception and state of mind of the patient. Self-report scales are often widely used when assessing depression in individuals, and are valuable when correlated to other objective measures.

Beck Depression Inventory II

The Beck Depression Inventory, originally introduced in 1961, is used in evaluating depressive symptoms in psychiatric patients as well as in normal populations. It is also one of the most widely used instruments in evaluating the severity of depressive symptoms (Whisman et al., 2000). The value of this instrument for evaluating patients with affective disorders lies in its high internal consistency among items despite the broad range of cognitive, affective, behavioral, and somatic symptoms thought to reflect the complexities of depression (Killgore, 1999). This inventory was updated to the Beck Depression Inventory-II (BDI-II) to reflect the diagnostic criteria for major depressive disorders as described by the DSM-IV (Steer et al., 1999).

The BDI-II is a self report inventory that assesses how a person has been feeling for the "last two weeks including today" according to the criteria set forth by the DSM-IV for major depressive episodes (Steer et al., 1999). The BDI-II is composed of 21 symptoms such as agitation, worthlessness, concentration difficulty, and loss of energy. Each of these symptoms is rated on a four-point scale ranging from 0-3, with the highest possible score being 63 (Steer et al., 1999). According to this scale, a score of 0-12 indicates minimal depression, 13-19 indicated mild depression, 20-28 indicates moderate depression, and 29-63 indicates severe depression.

The tests chosen for this research are widely used in clinical and research environments because they are easy to administer and have high internal validity. Serotonin is evident to be a contributor in disorders affecting the central nervous system. Some disorders related to serotonin also have auditory symptoms that compromise processing abilities of auditory information. Research in the area of serotonin related to auditory processing is necessary to because many patients are treated with SSRI medication. This research intends to add to a growing body of knowledge that is relevant to patients with auditory difficulty related to 5-HT dysfunction.

CHAPTER 3

METHODS

Subjects

All Groups

Thirty-five paid volunteers participated in this study, 17 in the control group and 18 in the experimental group. They were recruited from advertisements in the North Texas Daily newspaper, referrals from physicians, advertisements on the North Texas Television station (NTTV), as well as flyers placed around campus.

All subjects completed an informed consent explaining the procedures and tests, a case history, Beck Depression Inventory-II, and authorization for students to administer the testing. All subjects exhibited type A tympanograms. Each research participant was informed of confidentiality measures taken to maintain the integrity of a clinical research environment.

This project was sponsored by the Texas Advanced Research program, awarded to Dr. Kamakshi Gopal.

Inclusion Criteria for the Control Group

Subjects in the control group were included only if they had not taken an anti-depressant medication, had not been previously diagnosed with depression, or had ever been diagnosed with any mental illness related to serotonin including other affective disorders. All control subjects had normal hearing (American Academy of Ophthalmology and Otolaryngology, 1979).

Inclusion Criteria for Experimental Group

The experimental group consisted of subjects diagnosed with depression as specified by the criteria set forth by the prescribing physician and DSM-IV, followed by a prescription of one of the five SSRI medications; fluoxetine hydrochloride (Prozac), sertraline hydrochloride (Zoloft), paroxetine (Paxil), citalopram (Celexa), or fluvoxamine (Luvox). The experimental subjects were tested once when they were unmedicated for at least one month and the second time when they were on an SSRI for at least a month.

Subjects with history of head injury or other serious illnesses contraindicated to auditory or cognitive performance, or subjects taking any other central nervous system medication were not included in the study. Those subjects who were diagnosed with depression but not currently taking medication were included in the study and were first tested for the unmedicated round of testing. After they completed the unmedicated round these same subjects were re-tested when they began taking the SSRI for at least one month as prescribed by a physician. The once month period between testing sessions for the experimental group was based on the SSRI with the longest half-life, which is fluoxetine (Prozac) that has a half-life of 7-8 days.

The experimental subjects who were medicated first included those individuals planning to stop their SSRI medication with the consent of their doctor. Cessation of SSRI therapy was a voluntary event uninfluenced by this research. These subjects were tested first in a medicated condition. The same individuals were re-tested when they ceased taking medication for at least one month.

All people expressing interest in participating in this research were screened using a standard questionnaire. Their medication status, prescribing doctor, medical diagnosis,

other medications currently taken, and history of hearing loss were all considered when selecting this group. Cessation of any SSRI therapy was strictly voluntary and only subjects willing to be tested in both conditions were enrolled in the study. None of the subjects expressing interest in participation were excluded from the study for any reason.

Description of Experimental Procedures

Case History

Case history information was obtained from each subject prior to participation in test procedures. The case history, information consisted of routine history generally used in audiology clinics. In addition, it also included medical history such as history of depression and medications taken, audiologic history including hearing loss related to themselves and family members, and information regarding the prescribing physician of the SSRI.

Beck Depression Inventory-II

The Beck Depression Inventory-II is a self-questionnaire that addresses certain areas in a person's life and how those aspects of their life may change according to their depressive state. This 21-item inventory includes questions about sadness, guilty feelings, changes in sleeping and appetite, suicidal thoughts or wishes and other clinical symptoms of depression. This inventory was given to all experimental and control subjects. The BDI-II assesses how the person has been feeling for the last two weeks. The person evaluated is asked to circle the statement that best describes how they have been feeling for the last two weeks. The values assigned to the statements were added together to obtain a raw score. This score is then matched to a scale to assign a

particular level of depression; the highest score being 63 and the lowest being zero. According to this scale, a score of 0-12 indicates minimal depression, 13-19 indicated mild depression, 20-28 indicates moderate depression, and 29-63 indicates severe depression.

Otoscopy

Otoscopy is a visual observation of the external auditory meatus (EAM) and the tympanic membrane with an otoscope. The EAM was examined for excessive cerumen, foreign bodies, or any other abnormality. The tympanic membrane was assessed for any discoloration, perforations, or other indicators of a compromised tympanic membrane.

Each subject began the test battery with otoscopy to ensure their ear canals were healthy and there was no evidence of infection or other disorders of the external auditory meatus or the tympanic membrane.

Pure-Tone Audiometry

All subjects were tested using the modified Hughson -Westlake method of testing auditory thresholds (Carhart and Jerger, 1959). Thresholds were obtained at octave frequencies from 250 Hz to 8000 Hz. Bone conduction testing was preformed for any frequency falling outside the normal range of 25dB except for 8000 Hz. The Auricle (GN Otometrics, Bloomington, MN, USA) and the Orbiter 922 (GN Otometrics, Bloomington, MN, USA) were used for this procedure both using (Madsen, MX-41/AR, GN Otometrics, Bloomington, MN, USA) headphones.

Tympanometry

Tympanometry was preformed on each subject. Tympanograms give information about the integrity of the middle ear based on static compliance values. Tympanograms were classified according to Jerger (1970). Tympanometry was preformed using the GSI-33 (Grason-Stradler, Madison, WI, USA) to measure the patient's tympanic membrane mobility.

Acoustic Reflex Thresholds (ART)

Acoustic reflex thresholds were tested on both ears using a Grason-Stradler GSI-33 impedance bridge. Ipsilateral and contralateral reflexes were tested at 500, 1000, and 2000 Hz. Presentation began at 70 dBHL and increased by 5dB until a response was obtained. This measure was then repeated to obtain a response two out of three times. Presentation levels did not exceed 105 dB as to avoid potential noise induced hearing loss (Hunter et al., 1999). No response observed at this intensity level was recorded as no response (NR). Absent reflexes at 105 dB and recorded as NR were assigned arbitrary values of 115 dB to show the elevation or absence of the response.

Amplitude Resolution

Amplitude resolution was assessed using the Tucker Davis psychoacoustic equipment (Tucker-Davis Technologies, Gainesville, FL, USA). First, thresholds were obtained using the Hughson-Westlake procedure for 1000 Hz pure-tone. Following this, the test level was set at 30 dBSL. Two 1000 Hz, 500 ms tone pulses with a 200 ms interval were played binaurally in phase and began with the same intensity. Gradually, the second tone of the series increased in intensity by 0.5 dB until the subject indicated a change in the two tones presented (Fastl and Schorn, 1981; Fastl and Zwicker, 1979).

When the second tone was perceived as different at least two times, the computer program decreased the tone by 0.5dB. The subject continued responding by indicating if the two tones were same or different. The equipment was programmed to change the second 1000Hz pulse tone by 0.5 dB, either increasing or decreasing in intensity depending on the subject's response of same or different. When the subject indicated the tone was different, the intensity of the tone decreased until the subject indicated the tones sound the same. A reversal was counted when a listener reversed his/her judgment. The computer averaged the number of reversals over 60 trials to obtain the reversal average. This indicated the average increase in decibel level for the person to notice a change in the amplitude of the stimulus.

Auditory Brainstem Response

The auditory brainstem response (ABR) was elicited using binaural alternating clicks at a rate of 21.1 per second using the Bio-logic Navigator System (Bio-Logic Systems, Corp., Mundelein, IL, USA). Cup electrodes were placed at four different locations using the 10-20 international electrode system (Hall, 1990). The non-inverting electrode was placed at FPz, the inverting electrode was placed at the nape of the neck, and the nasion was used for the grounding electrode placement. Impedance was maintained at 1000 ohms for all subjects. The stimulus was delivered binaurally using foam tipped insert earphones. The responses were averaged over 1024 runs.

The protocol began at 70dBnHL and descended until threshold was reached. Thresholds were determined by a repeatable wave V at the lowest intensity. Repeatable responses exhibiting good morphology and low artifacts were considered true responses

(Hall, 1990). When threshold was reached the ABR recordings were made at 55 dBnSL. Each recording was repeated twice to ensure a true response.

The latencies and amplitudes for ABR peak V were measured. Identification of waves were rechecked independently by another examiner.

Auditory Late Response

The auditory late response used the same equipment procedures and equipment as the auditory brainstem response. Stimuli used for the ALR included rarefacting tone burst at a rate of 1.1 per second. Responses represent the average for 150 responses, and were repeated to ensure reliable and repeatable responses.

The ALR protocol included testing at 15, 25, 35, 45, and 55 dBnSL levels in a random order using the threshold from the ABR. ALRs were repeated at each intensity to ensure a true response. Subjects remained awake and alert throughout the course of the test. Patients who were sleepy were not tested at that time and were rescheduled for a different time of the day when they were more alert.

The latency and amplitude measures were made for P2 and N1 components of the ALR. This data, similar to the ABR data, was crosschecked by another researcher to ensure reliability.

Reliability

The tests used for this research were chosen for their ease of administration as well as their reliability. Each patient participated in the same protocol although tests were randomized to maintain effective research design. Pure-tone audiometry, and acoustic reflexes used the bracketing procedure where two out of three responses were identified as threshold. Amplitude resolution has an internal reliability calculated by reversals averaged over 60 trials. Auditory evoked responses were measured using standard electrode placement and with electrode impedance at 1000 ohms. The responses were measured over 1024 times for brainstem responses and 150 times for cortical responses. Identification of waveforms were done by one researcher then checked by another who was unaware of the subject's condition or group membership.

Statistical Analysis

Statistical analysis of this data was done using Statistics Program for Social Sciences (SPSS) software (SPSS, Inc., Chicago, IL, USA). Mean and standard deviation values were obtained on all test scores. Independent sample t-tests were used to compare the results between control and unmedicated groups, and between control and medicated groups. Paired-comparison t-test was used to evaluate the differences between the medicated and unmedicated conditions for the experimental group. The criterion adopted for significance was $\alpha = 0.05/n$ where n= number of dependent variables compared (Dunn, 1961).

CHAPTER 4

RESULTS AND DISCUSSION

Results

The purpose of this study was to investigate the role of SSRI medication on the auditory system in subjects diagnosed with clinical depression. The measures investigated in this study included otoscopy, pure tone audiometry, tympanometry, acoustic reflex thresholds (ARTs), amplitude resolution, auditory brainstem response (ABR), auditory late response (ALR), and the Beck Depression Inventory-II (BDI-II). Thirty-five subjects participated in this research, 17 in the control group and 18 in the experimental group. The experimental group in this study participated in two rounds of testing which included a medicated condition and an unmedicated condition. The control group consisted of subjects not presenting with depression, nor had any history of an affective disorder, or treatment with SSRI medication.

Otoscopy and Tympanometry

Otoscopy revealed clear ear canals in all subjects. Tympanometry revealed Type A tympanograms in 33 of the 35 subjects included in this study suggesting normal middle ear function. Two subjects presented with Type Ad tympanograms, one in the control group and one in the experimental group. Review of the case history for both subjects revealed a history of middle ear infections as children with insertion of PE tubes during childhood in one of the subjects. However, upon inspection of pure tone audiometry, both of these subjects exhibited normal hearing with thresholds below 25 dBHL.

All subject included in this study had pure tone averages (PTA) below 25 dBHL which is within the normal range of hearing for adults (AAOO, 1979). The mean age, and PTA for both experimental and control groups are listed in Table 1. Raw data for these results can be found in Table Appendix A.

Table 1: Results of basic measures: age, otoscopy, tympanograms

Measure	Control Group	Experimental Group	
	Control	Medicated Condition	Unmedicated Condition
Group Size	N= 17	N= 18	N=18
Age (years)	Mean: 25.24 S.D.: 3.75	Mean: 26.39 S.D.: 9.80	Mean: 26.39 S.D.: 9.80
Otoscopy	Normal for all subjects	Normal for all subjects	Normal for all subjects
Tympanometry	All type A except for one subject with type Ad/Ad	All type A except for one subject with type Ad/Ad	All type A except for one subject with type Ad/Ad
PTA	Mean: 3.32 S.D.: 1.72	Mean: 7.96 S.D.: 6.18	Mean: 7.80 S.D.: 7.13

Acoustic Reflex Thresholds

The acoustic reflex threshold (ART) measures the contraction of the stapedius muscle in the middle ear to sufficiently loud stimuli. Contraction of the stapedius muscled was measured ipsilaterally and contralaterally for tones at 500, 1000, and 2000 Hz. Responses were recorded as threshold for the lowest intensity of a pure tone that brought about a change in compliance of 0.03 ohms. Absent reflexes at the limit of testing 105 dB (Hunter et al., 1999) were recorded as no response (NR) and then assigned an arbitrary value of 115 dB to show the response as elevated. This is likely to affect the means and standard deviations, either increasing or decreasing the values. The

ipsilateral and contralateral values for individual frequencies were averaged separately for each ear.

Means and standard deviations for the averages of these specific conditions were calculated. Table 2 shows the mean and standard deviation scores with the experimental group during medicated and unmedicated conditions as well as the scores from the control group. (NR means NR @ 105dBHL) No significant differences were found between the groups for right or left ears ($p > 0.05$).

Table 2: Averaged Acoustic Reflex Thresholds (dBHL) for control and experimental conditions (medicated and unmedicated)
Ipsi= Ipsilateral, Contra = Contralateral

Condition	Control Condition	Medicated Condition	Unmedicated Condition
Group Size	N= 17	N= 18	N=18
R Ipsi	Mean: 92.94 S.D.: 9.49	Mean: 94.51 S.D.: 8.14	Mean: 93.73 S.D.: 8.87
R Contra	Mean: 100.10 S.D.: 9.99	Mean: 101.86 S.D.: 9.05	Mean: 99.74 S.D.: 8.25
L Ipsi	Mean: 94.90 S.D.: 12.04	Mean: 93.33 S.D.: 8.08	Mean: 91.76 S.D.: 7.85
L Contra	Mean: 103.24 S.D.: 10.28	Mean: 100.65 S.D.: 8.48	Mean: 99.63 S.D.: 6.51

A paired-samples t-test between medicated and unmedicated conditions did not show significant differences for acoustic reflexes. The p values for this comparison ranged for the right ear from 0.166-0.646 and for the left ear p values ranged between 0.061-0.884. Raw data for acoustic reflexes can be found in Appendix C.

Amplitude Resolution

Amplitude resolution, which measures a person's ability to detect small changes in intensity, was measured in 0.5 dB steps. Two 1000 Hz tone pulses with duration of 500 ms separated by a 200ms interval of silence were played binaurally. The subject's indication of whether the tones were the same or different, helped determine the average intensity needed to discriminate a change in intensity.

Table 3 shows the mean and standard deviation for these relationships between the control and experimental groups. Significant differences were not observed between the control group and medicated group, nor were they observed for the control group and the unmedicated group. The paired-samples t-test between the medicated and unmedicated group also showed no significant differences. It was also noted that the unmedicated group had the widest standard deviation followed by the medicated group. Raw data for reversals can be found in Appendix D.

Table 3: Reversals for the control group compared to experimental group.

Reversals	Control Condition	Medicated Condition	Unmedicated Condition
Group Size	N= 17	N= 17	N=16
Reversal	Mean: 2.79 S.D.: .99	Mean: 2.42 S.D.: 1.49	Mean: 2.61 S.D.: 2.51

Beck Depression Inventory-II

The Beck Depression Inventory-II (BDI-II) was used to assess the level of depression in each subject using the criteria mandated by the test. According to this

criteria, a score of 0-12 indicates minimal depression, 13-19 indicates mild depression, 20-28 indicates moderate depression, and 29-63 indicates severe depression. All subjects in the control group and subjects in both conditions of the experimental group were given the BDI-II.

Table 4 shows the relationships between the groups compared for level of depression. Significant differences were observed between the control group and the experimental group in the medicated condition ($p = 0.000$) as well as between the control group and experimental group in the unmedicated group ($p = 0.000$). Overall, the unmediated group showed the highest mean scores with a mean of 15.24 with and a range of 36. Comparison between the medicated and unmedicated conditions, however, did not reveal significant differences ($p > 0.05$). According to the scale the medicated and the unmediated group showed mild depression where the control group showed minimal depression. Raw data for the BDI-II can be found in Appendix E.

Table 4: Mean of BDI-II scores for all group comparisons

Condition	Control Condition	Medicated Condition	Unmedicated Condition
Group Size	N= 16	N= 17	N=17
BDI-II Score Value	Mean: 1.44 S.D.: .2.0	Mean: 14.12 S.D.: 9.12	Mean: 15.24 S.D.: 13.20

Auditory Brainstem Response

Peak V Latency

The auditory brainstem response was measured to assess the integrity of the auditory pathway from the VIIIth nerve to the midbrain. ABR thresholds for all subjects fell within normal limits (<20 dBnHL). Amplitudes and latencies were measured at 55dBnSL, for peak V which is generated at the level of the lateral lemniscus in humans. The control group was first compared to the experimental group. No significant differences were observed for the latency of peak V at 55 dBnSL between the control group as compared to the medicated group, or the control group as compared with the unmedicated group. Likewise, when the medicated condition of the experimental group was compared to the unmedicated condition no significant differences were observed. Table 5 shows the mean and standard deviation values for the latency of peak V. Raw data for the latencies of ABR peak V can be found in Appendix F.

Table 5: Mean Latencies for ABR Peak V

ABR	Control Condition	Medicated Condition	Unmedicated Condition
Group Size	N= 17	N= 18	N= 18
Peak V Latency in milliseconds	Mean: 5.67 S.D.: 0.24	Mean: 5.64 S.D.: 0.21	Mean: 5.67 S.D.: 0.21

Amplitude of Peak V

The amplitudes of ABR peak V at 55 dBnSL were also compared between groups. No significant differences were found for the amplitudes between the control

group and the medicated group, or for the control group and unmedicated group. When the two experimental conditions were compared no significant differences were found for the amplitude of peak V. Table 6 shows the mean and standard deviation values for the amplitude of wave V. Although the medicated and unmedicated groups showed larger amplitudes, no significant differences were observed for any of the groups. Raw data for the amplitudes of ABR peak V can be found in Appendix F.

Table 6: Mean Amplitudes for ABR Peak V

ABR	Control Condition	Medicated Condition	Unmedicated Condition
Group Size	N= 17	N= 18	N= 18
Peak V Amplitude in microvolts	Mean: 0.94 S.D.: 0.25	Mean: 1.03 S.D.: 0.26	Mean: 1.00 S.D.: 0.30

Auditory Late Responses

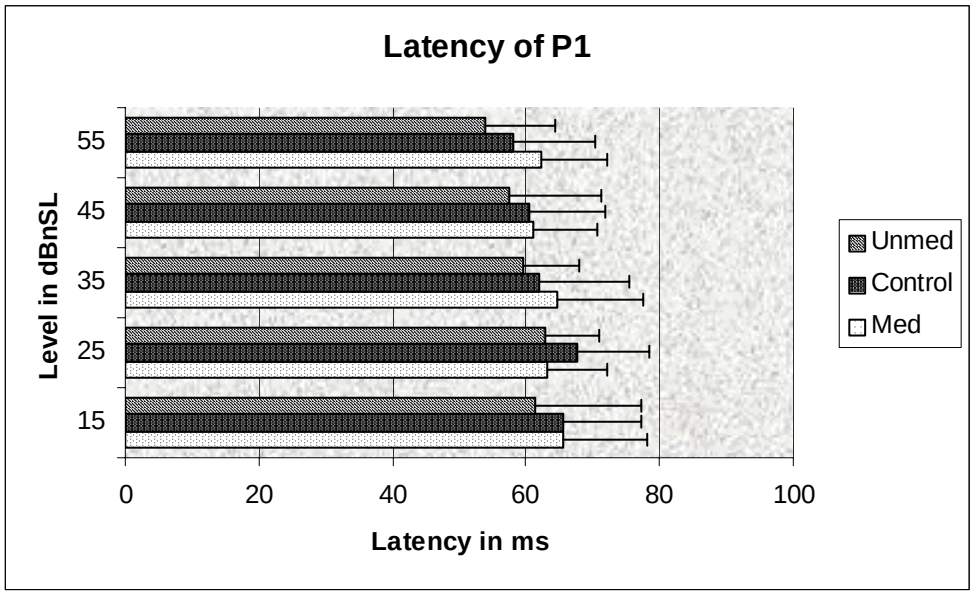
The auditory late response (ALR) generated at the level of the primary auditory cortex occurs between 50-300 ms and is identified as P1, N1and P2 components. Latencies and amplitudes of these peaks were compared between medicated and unmedicated conditions as well as between the control and experimental groups. The five intensities tested were 55dBnSL, 45dBnSL, 35dBnSL, 25dBnSL, and 15dBnSL.

Latency of P1

The latency of P1 was measured for all subjects at all five intensity levels. The control group was first compared to the experimental group. Independent sample t-test between the control and medicated group did not reveal any significant differences for any of the intensities. When the control group was compared to the unmedicated group,

significant differences were not observed, however, the unmedicated group consistently had shorter latencies when compared to the control group. The mean and standard deviation values for P1 latency can be viewed in Figure 1.

Figure 1: Latency of P1 in control and experimental groups (medicated & unmedicated condition)



The latency of P1 was also compared between the two conditions within the experimental group. Unmedicated subjects showed consistently shorter latencies at all intensities when compared to the medicated condition. Paired comparison t-test between the medicated and unmedicated conditions revealed a significantly shorter latency for P1 at 55dBnSL (p= 0. 001).

Amplitude of P1/N1

The amplitude of P1/N1 was measured for the five intensities that define the amplitude stimulus intensity function; 55dBnSL, 45dBnSL, 35dBnSL, 25dBnSL, and 15dBnSL. The independent t-test comparing the control group to the medicated condition did not reveal any significant differences at any of the intensities. The independent t-test also did not reveal significant differences between the control group and the unmedicated group. Paired-sample t-test of the experimental conditions did not reach significance for any of the intensities in the series.

Table 7: P1/N1 Amplitude (μv) between control and experimental groups (medicated and unmedicated)

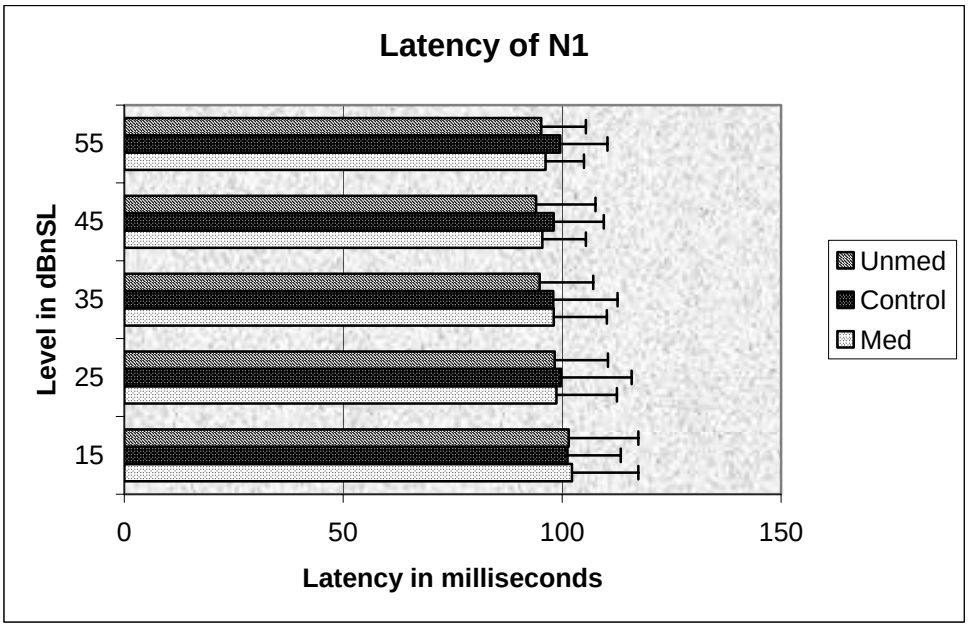
P1 Amplitude	Control Condition	Medicated Condition	Unmedicated Condition
Group Size	N= 17	N= 18	N= 18
55 dBnSL	Mean: 3.38 S.D.: 1.26	Mean: 3.41 S.D.: 1.82	Mean: 3.17 S.D.: 1.68
45 dBnSL	Mean: 2.64 S.D.: 1.16	Mean: 3.09 S.D.: 1.38	Mean: 3.02 S.D.: 1.31
35 dBnSL	Mean: 2.13 S.D.: 0.92	Mean: 2.66 S.D.: 1.18	Mean: 2.43 S.D.: 1.19
25 dBnSL	Mean: 2.15 S.D.: 1.29	Mean: 2.36 S.D.: 1.43	Mean: 2.09 S.D.: 1.24
15 dBnSL	Mean: 2.33 S.D.: 0.17	Mean: 2.17 S.D.: 1.35	Mean: 2.03 S.D.: 1.21

Latency of N1

The latency of N1 was measured for all five intensities as set forth in the protocol. Comparisons were first made between the control and experimental groups. Figure 2 shows the mean and standard deviation values for the latency of N1. No significant

differences were observed for the control group and the medicated condition at any of the intensities. Similarly, no significant differences were observed for the control group and unmedicated condition.

Figure 2: Mean N1 Latency for control and experimental groups (medicated & unmedicated)



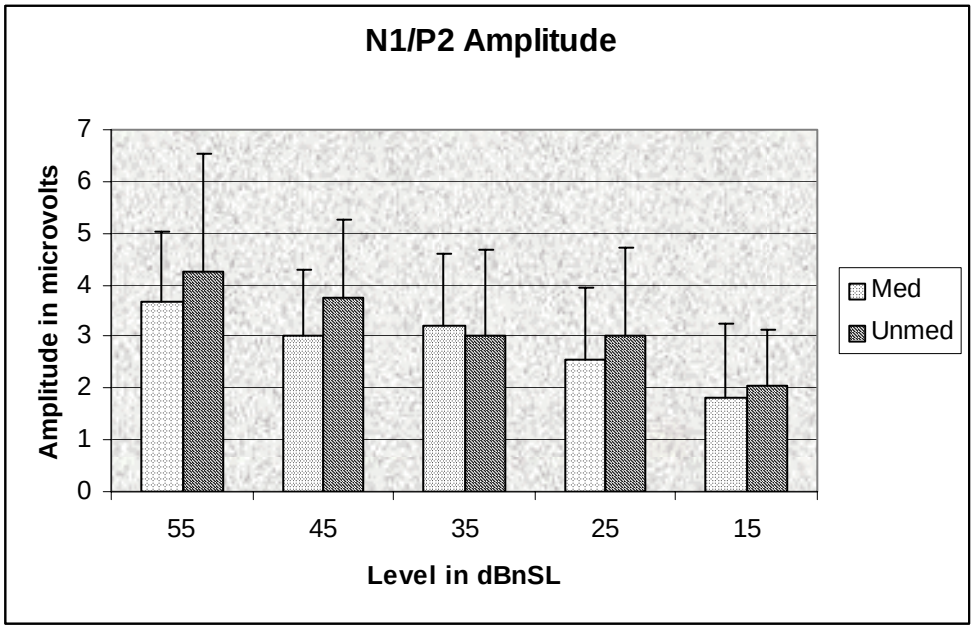
The latencies of N1 were compared within the experimental group using the paired-samples t-test. Significant differences were not reached for any of the intensities tested, though consistently the unmedicated condition showed shorter latencies when compared to the medicated condition.

Amplitude of N1/P2

The amplitude of this peak was measured for all intensities from 55dBnSL to 15dBnSL and compared between control group and experimental group. These independent samples t-test did not reveal significant differences between the control

group and the medicated condition. Similarly, no significant difference was observed between the control group and the unmedicated group. When the N1/P2 amplitude was compared between the medicated and unmedicated conditions, amplitudes for the unmedicated condition were greater than the medicated condition at all intensities tested except one (35dBnSL). A paired comparison t-test showed significant difference only at 45 dBnSL (p=0.008). This is shown in Figure 3.

Figure 3: Mean N1/P2 Amplitude for the experimental group (medicated and unmedicated)



The amplitude/intensity growth between 15dBnSL and 55dBnSL is shown in Table 8 for all groups. The unmedicated group showed a larger amplitude growth than the control group. It was interesting to see that the same subjects while under SSRI medication showed less amplitude growth.

Table 8: P1/N1 Amplitude growth (μv) between control and experimental groups (medicated and unmedicated)

Condition	Control Condition	Medicated Condition	Unmedicated Condition
Group Size	N= 17	N= 18	N= 18
Difference 55-15 dBnSL	2.09 μv	1.72 μv	2.32 μv

Discussion

The purpose of this research was to investigate the relationship between SSRI medication and auditory skills in clinically depressed subjects. The tests used in this research included acoustic reflexes, amplitude resolution, ABR latencies and amplitude of peak V, ALR latencies of P1 and N1, and ALR amplitudes for P1/N1 and N1/P2. The selection of tests was based on available clinical research of serotonin related disorders and the its relationship to auditory processing. Other auditory measures such as pure tone thresholds and otoscopy were used to examine the sensitivity and integrity of the auditory system. The BDI-II was used to assess the degrees of depression exhibited by experimental subjects as compared to the control group.

All subjects in this research exhibited normal hearing. All subjects exhibited normal type A tympanograms except for two subjects who showed type Ad tympanograms. These subjects reported to have middle ear infections during childhood. Middle ear infections can sometimes cause excessive scarring of the tympanic membrane resulting in shallow tympanograms. These infections can also cause thinning of the

tympanic membrane or monomeric membranes, which are more compliant and will result in type Ad tympanograms.

The acoustic reflex pathway consists of some of the same auditory nuclei as the ABR pathway (Thompson, 1983) and therefore like the ABR, has a concentration of serotonergic fibers. Hence, the ART was used to assess the involvement of serotonin at the level of the brainstem. No significant differences were observed for acoustic reflex thresholds for any of the groups for ipsilateral or contralateral conditions. Carney (2001) also showed no significant differences in her static group comparison study for the acoustic reflex threshold or any other measure involving the acoustic reflex arc pathway. SSRI did not appear to have any influence on the acoustic reflex thresholds. Serotonin may not play a significant role at the level of the brainstem in humans.

In this study amplitude resolution did not show significant differences between any of the groups compared. Carney (2001) showed in the static group comparison that ones ability to detect small changes in intensity was not affected by SSRI medication.

The BDI-II revealed significant differences between the control group and experimental group in both conditions. The unmedicated condition had worse scores when compared to any other group, though still only exhibiting mild depression. The scores for the BDI-II did not differ significantly between the unmedicated and the medicated condition and in a few cases the scores for the medicated condition increased..

The latency and amplitude of ABR Peak V did not reveal significant differences for any of the groups compared. Bishop (2001) also did not show significant differences between the static group comparison for ABR peak V for latency or amplitude. Though

all subjects exhibited normal ABR thresholds based on Peak V amplitude and latency data, all groups showed an increase in amplitude as intensity increased.

The latency of P1 was significantly shorter for the experimental condition as compared to the control group. A pattern of consistently shorter latencies for all intensities tested as part of an intensity series in 10 dB steps from 15dBnSL- 55dBnSL was observed for the unmedicated condition as compared with the control condition. This pattern can also be seen when comparing the unmedicated condition to the control group. Research by Concu et al. (1977) showed latencies in the early component evoked potentials in rats to decrease when levels of cerebral serotonin decreased. Serotonin is a modulator in the auditory system and serves to fine tune sensory information in the afferent auditory pathway. When the level of cerebral serotonin is decreased, a decrease in latency is also observed. This is a result of less inhibition and consequently less control over the sensory input traveling along the auditory pathway. In this study the experimental group showed a lengthening of the P1 latency with SSRI medication.

Although significant differences were not obtained for the latency of N1, the pattern of shorter latencies for the unmedicated group as compared to the control group is distinct. The N1 pattern of shorter latencies also is pronounced for the unmedicated group when compared to the medicated group. Similar to the latency of P1, shorter transmissions speeds are attributed to less inhibition in the auditory pathway, and observed in cases with lower levels of serotonin.

Significant differences were observed for the N1/P2 amplitude at 45dBnSL for the unmedicated group when compared to the control group. It is evident from exploiting the difference in amplitudes between intensities that the subjects in the unmedicated

group exhibit a rapid increase in amplitude at the higher intensities. An increase in amplitude due to stimulus intensity is also observed for the unmedicated group as compared to the control group suggesting less control of the inhibitory mechanism. This is referred to as the amplitude-stimulus augmentation function as described by Hegerl and Juckel (1993). The amplitude stimulus intensity function has been debated to exist by several researchers (Hegerl & Juckel, 1993; Juckel et al., 1999) and argued not observable by others (Dierks et al., 1999; Debener et al., 2002). It appears that serotonin is active in the auditory cortex and contributes to the amplitude stimulus intensity function. Further, as suggested by Juckel et al. (1999) by identifying the augmenting effect of the N1/P2 component, patients exhibiting serotonin disorders could more efficiently and specifically be treated with regard to medication response rather than the trial and error approach currently practiced. It appears more research in this area is necessary to further establish this landmark of the ALR.

Some of these trends that do not reach significant differences may be due to the relatively small sample size. Further, more defined trends might be observed by increasing the homogeneity of the groups by matching subjects by degrees of depression exhibited or specific medications taken. It appears the only significant differences observed for the electrophysiology battery was above the level of the brainstem at the cortical level. Serotonin may show effects at the cortical level and might not play a significant role in the peripheral auditory system, which explains why no significant differences were observed for the ABR between the groups studied.

Conclusions

The purpose of this research was to investigate the effect of SSRI medication on the auditory system in clinically depressed subjects. The tests used in this research are widely accepted clinical measures and have been used in other studies relevant to research related to disorders of serotonin. This protocol consisted of basic auditory measures such as otoscopy, tympanometry, and pure tone audiometry, as well as more advanced measures, which included ART, amplitude resolution, ABR, and ALR. The BDI-II was used in this research to establish degrees of depression exhibited by subjects in the experimental group. Results from these test measures indicate a series of consistent trends and statistically significant differences for several of the tests. The following statistically significant findings were observed:

- The experimental group exhibited greater scores on the BDI-II than did the control group for both medicated and unmedicated conditions.
- The unmedicated group had shorter latencies at 55 dBnSL for P1 of the ALR compared to the medicated group.
- The unmedicated group exhibited greater amplitudes at 45 dBnSL than did the medicated group for the N1/P2 amplitude.

The following trends were observed:

- The unmediated group showed shorter latencies for ALR Peak P1 and N1, compared to the control and medicated group.

- The unmedicated condition of the experimental group showed a greater growth in amplitude for the N1/P2 component as compared to the control group and medicated condition.

Results from this research indicate that SSRI medication influences auditory processing at a level superior to the brainstem. This is indicative in the decrease in latencies of ALR P1 and N1 as well as an increase in amplitude at higher intensities for the unmedicated subjects. Central serotonin in the unmedicated subjects may have been depleted resulting in less inhibition or control causing the amplitudes to augment and the latencies to decrease.

RECOMMENDATIONS FOR FUTURE RESEARCH

Recommendations for future research include an increased sample size to further distinguish patterns seen between unmedicated and control groups as well as observed between medicated and unmedicated groups. Also recommended for future research for SSRI medication and auditory measures include a more homogenous sample that might include subjects taking the same SSRI and same dosages, or subjects matched for degree of depression as established by the BDI-II. The tests employed in this research are sensitive to subtle changes in the auditory system that may be more observable when variability between subjects is decreased by increasing the sample size and homogeneity of the groups. Refining these measures more and using them systematically in a psychiatric clinic could possibly help determine the efficacy of treatment in individuals taking SSRI medication.

Also ear-specific measures were not obtained in most test measures, so it is recommended that ear-specific tests be carried out in the future. It is apparent that future research related to serotonin in the auditory system is warranted. However, because of the complicated nature of depression and other affective disorders coupled with the many roles serotonin plays in the body and nervous system, research designs must take into account the variability that will naturally exist between subjects and between groups.

APPENDIX A

DESCRIPTIVE INFORMATION

Subject Number	Age	Avg PTA	Tymps R/L	SSRI	Diagnosis	Dosage Mg/Day
C1	24.00	5.00	A/A			
C2	31.00	4.50	A/A			
C3	22.00	7.50	Ad/Ad			
C4	21.00	3.50	A/A			
C5	23.00	3.50	A/A			
C6	23.00	5.00	A/A			
C7	23.00	2.00	A/A			
C8	23.00	2.00	A/A			
C9	32.00	0.00	A/A			
C10	23.00	4.00	A/A			
C11	23.00	1.50	A/A			
C12	28.00	1.00	A/A			
C13	34.00	0.00	A/A			
C14	25.00	1.00	A/A			
C15	24.00	3.00	A/A			
C16	25.00	9.00	A/A			
C17	25.00	4.00	A/A			
E1- med	20.00	7.50	A/A	Zoloft	Depression	50 MG
E2-med	26.00	7.50	A/A	Zoloft	Depression	100 MG
E3-med	21.00	9.00	A/A	Prozac	Depression	40 MG
E4-med	21.00	6.00	A/A	Zoloft	Depression	50 MG
E5-med	32.00	1.50	A/A	Zoloft	Depression	100 MG
E6-med	27.00	20.00	A/A	Zoloft	Depression	50 MG
E7-med	29.00	6.00	A/A	Prozac	Depression	40 MG
E9-med	19.00	19.00	A/A	Prozac	Depression	20 MG
E10-med	18.00	2.00	Ad/Ad	Prozac	Depression	20 MG
E11-med	23.00	4.00	A/A	Paxil	Anxiety	No Data
E12-med	19.00	3.00	A/A	Prozac	Depression	10 MG
E13-med	22.00	3.00	A/A	Zoloft	Depression	50 MG
E14-med	42.00	5.00	A/A	Zoloft	Depression	150 M
E15-med	23.00	17.00	A/A	Prozac	Depression	20 MG
E16-med	27.00	3.50	A/A	Zoloft	OCD/ADD	unknown
E17-med	21.00	6.50	A/A	Celexa	Depression	10 MG
E18-med	58.00	18.35	A/A	Prozac	Depression	40 MG
E19-med	27.00	4.50	A/A	Zoloft	Depression	100 MG
E1-unmed	20.00	6.00	A/A			
E2-unmed	26.00	3.00	A/A			
E3-unmed	21.00	5.00	A/A			
E4-unmed	21.00	4.00	A/A			
E5-unmed	32.00	1.00	A/A			
E6-unmed	27.00	21.00	A/A			
E7-unmed	29.00	6.00	A/A			
E9-unmed	19.00	22.50	A/A			
E10-unmed	18.00	2.50	Ad/Ad			
E11-unmed	23.00	5.00	A/A			
E12-unmed	19.00	5.50	A/A			
E13-unmed	22.00	2.50	A/A			
E14-unmed	42.00	2.50	A/A			
E15-unmed	23.00	17.00	A/A			
E16-unmed	27.00	4.00	A/A			
E17-unmed	27.00	7.00	A/A			
E18-unmed	58.00	20.85	A/A			
E19-unmed	27.00	5.00	A/A			

[1] Subject number E-8 was not included in this research.

APPENDIX B

SSRI BENEFIT FORM

SSRI BENEFIT FORM

Name: _____ Date: _____

Age: _____ Phone: _____

Please answer the following questions as best you can.

1. Medical diagnosis: Depression _____ Migraine _____

Other _____

2. Name of SSRI medication you are currently taking (Celexa, Prozac, Zoloft, Luvox, Paxil).

_____

3. Daily dosage: _____mg/day. How long have you been on this medication?

_____

4. SSRI prescribing physician _____ Location of your physician's

medical office _____

5. List other medications, including any herbal supplements, such as **St. John's Wort**:

_____

6. Have you noticed any change in your auditory sensitivity and understanding speech since taking SSRI medication?

_____

7. It is essential for our research to understand how this medication is affecting you. Please describe in your own words how you feel the medication **is** and/or **is not** helping you with your symptoms.

_____

_____

_____

_____

APPENDIX C

ACOUSTIC REFLEX THRESHOLDS

Subject Number	R- Ipsi .5K	R- Ipsi 1K	R-Ipsi 2K	Avg R-Ipsi	R-Contra .5K	R-Contra 1K	R-Contra 2K	Avg R-Contra	R-CP	RCS	RC Ipsi
C1	95.00	85.00	85.00	88.33	95.00	90.00	90.00	91.67	100.00	95.00	115.00
C2	85.00	80.00	85.00	83.33	100.00	90.00	95.00	95.00	105.00	90.00	110.00
C3	95.00	90.00	85.00	90.00	100.00	100.00	95.00	98.33	115.00	95.00	115.00
C4	95.00	85.00	90.00	90.00	100.00	90.00		95.00	100.00	80.00	110.00
C5	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00
C6	85.00	85.00	85.00	85.00	95.00	90.00	95.00	93.33	80.00	95.00	105.00
C7	105.00	105.00	95.00	101.67	115.00	115.00	105.00	111.67	115.00	100.00	115.00
C8	85.00	85.00	80.00	83.33	100.00	100.00	85.00	95.00	85.00	90.00	100.00
C9	95.00	90.00	85.00	90.00	105.00	100.00	90.00	98.33	115.00	100.00	115.00
C10	115.00	105.00	105.00	108.33	115.00	115.00	115.00	115.00	115.00	115.00	115.00
C11	100.00	95.00	100.00	98.33	115.00	115.00	115.00	115.00	115.00	115.00	115.00
C12	90.00	90.00	95.00	91.67	100.00	95.00	100.00	98.33	105.00	105.00	115.00
C13	100.00	95.00	95.00	96.67	100.00	95.00	90.00	95.00	115.00	115.00	115.00
C14	85.00	80.00	90.00	85.00	100.00	90.00	90.00	93.33	100.00	90.00	110.00
C15	85.00	80.00	85.00	83.33	85.00	90.00	85.00	86.67	90.00	85.00	100.00
C16	105.00	100.00	105.00	103.33	115.00	115.00	115.00	115.00	115.00	110.00	115.00
C17	90.00	85.00	85.00	86.67	95.00	90.00	85.00	90.00	95.00	85.00	115.00
E1- med	105.00	95.00	110.00	103.33	110.00	95.00	105.00	103.33	115.00	115.00	115.00
E2-med	90.00	85.00	90.00	88.33	100.00	95.00	95.00	96.67	105.00	90.00	105.00
E3-med	90.00	90.00	95.00	91.67	100.00	95.00	95.00	96.67	115.00	115.00	115.00
E4-med	95.00	95.00	95.00	95.00	105.00	100.00	115.00	106.67	115.00	115.00	115.00
E5-med	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00
E6-med	90.00	90.00	90.00	90.00	100.00	100.00	95.00	98.33	115.00	105.00	115.00
E7-med	100.00	100.00	100.00	100.00	105.00	105.00	95.00	101.67	115.00	105.00	115.00
E9-med	95.00	95.00	90.00	93.33	100.00	100.00	100.00	100.00	115.00	115.00	115.00
E10-med	85.00	85.00	100.00	90.00	115.00	115.00	115.00	115.00	90.00	90.00	115.00
E11-med	80.00	80.00	85.00	81.67	105.00	95.00	90.00	96.67	105.00	95.00	105.00
E12-med	95.00	95.00	90.00	93.33	105.00	95.00	90.00	96.67	100.00	100.00	115.00
E13-med											
E14-med	85.00	85.00	90.00	86.67	95.00	90.00	90.00	91.67	115.00	105.00	115.00
E15-med	95.00	100.00	100.00	98.33	115.00	115.00	115.00	115.00	115.00	115.00	115.00
E16-med	95.00	95.00	95.00	95.00	115.00	100.00	100.00	105.00	115.00	115.00	115.00
E17-med	115.00	95.00	105.00	105.00	115.00	115.00	115.00	115.00	105.00	115.00	115.00
E18-med	85.00	85.00	85.00	85.00	90.00	85.00	80.00	85.00	90.00	80.00	110.00
E19-med	95.00	95.00	95.00	95.00	95.00	95.00	90.00	93.33	100.00	85.00	115.00
E1-unmed	90.00	85.00	100.00	91.67	95.00	85.00	90.00	90.00	115.00	115.00	115.00
E2-unmed	95.00	90.00	95.00	93.33	100.00	105.00	100.00	101.67	105.00	90.00	105.00
E3-unmed	90.00	95.00	95.00	93.33	100.00	100.00	95.00	98.33	115.00	115.00	115.00
E4-unmed	95.00	90.00	90.00	91.67	115.00	105.00	100.00	106.67	115.00	115.00	115.00
E5-unmed	115.00	105.00	105.00	108.33	115.00	105.00	105.00	108.33	115.00	115.00	115.00
E6-unmed	80.00	85.00	80.00	81.67	90.00	90.00	90.00	90.00	115.00	95.00	95.00
E7-unmed	115.00	100.00	105.00	106.67	115.00	105.00	100.00	106.67	115.00	115.00	115.00
E9-unmed	100.00	95.00	95.00	96.67	115.00	105.00	100.00	106.67	115.00	115.00	115.00
E10-unmed									105.00	85.00	115.00
E11-unmed	85.00	85.00	85.00	85.00	100.00	90.00	85.00	91.67	90.00	90.00	105.00
E12-unmed	95.00	90.00	85.00	90.00	100.00	95.00	90.00	95.00	95.00	90.00	105.00
E13-unmed	85.00	90.00	95.00	90.00	115.00	95.00	95.00	101.67	115.00	115.00	115.00
E14-unmed	85.00	85.00	85.00	85.00	95.00	85.00	90.00	90.00	110.00	105.00	115.00
E15-unmed	90.00	90.00	85.00	88.33	105.00	105.00	105.00	105.00	100.00	100.00	90.00
E16-unmed	95.00	95.00	95.00	95.00	115.00	100.00	95.00	103.33	115.00	105.00	105.00
E17-unmed	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00
E18-unmed	85.00	85.00	90.00	86.67	90.00	85.00	80.00	85.00	95.00	85.00	110.00
E19-unmed	85.00	100.00	100.00	95.00	105.00	95.00	100.00	100.00	115.00	115.00	115.00

Subject Number	L- Ipsi .5K	L- Ipsi 1K	L-Ipsi 2K	Avg L-Ipsi	L-Contra .5K	L-Contra 1K	L-Contra 2K	Avg L-Contra	LCP	LCS	LC Ipsi
C1	90.00	90.00	90.00	90.00	95.00	100.00	95.00	96.67	100.00	95.00	115.00
C2	85.00	80.00	80.00	81.67	90.00	90.00	95.00	91.67	100.00	95.00	115.00
C3	100.00	100.00	105.00	101.67	115.00	115.00	115.00	115.00	115.00	115.00	115.00
C4	85.00	80.00	80.00	81.67	95.00	90.00	85.00	90.00	95.00	80.00	110.00
C5	105.00	100.00	105.00	103.33	115.00	115.00	115.00	115.00	115.00	105.00	105.00
C6	85.00	90.00	90.00	88.33	95.00	85.00	90.00	90.00	105.00	90.00	105.00
C7	85.00	80.00	85.00	83.33	105.00	90.00	85.00	93.33	100.00	90.00	105.00
C8	75.00	75.00	80.00	76.67	100.00	95.00	85.00	93.33	90.00	85.00	100.00
C9	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00
C10	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00
C11	95.00	100.00	105.00	100.00	115.00	115.00	100.00	110.00	115.00	115.00	115.00
C12	85.00	95.00	100.00	93.33	105.00	100.00	115.00	106.67	115.00	105.00	115.00
C13	95.00	95.00	95.00	95.00	115.00	105.00	115.00	111.67	115.00	115.00	115.00
C14	95.00	95.00	95.00	95.00	105.00	90.00	105.00	100.00	110.00	100.00	115.00
C15	90.00	95.00	90.00	91.67	105.00	105.00	105.00	105.00	115.00	115.00	115.00
C16	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00	110.00	115.00
C17	90.00	85.00	85.00	86.67	95.00	90.00	90.00	91.67	90.00	105.00	115.00
E1- med	100.00	90.00	100.00	96.67	105.00	105.00	100.00	103.33	115.00	115.00	115.00
E2-med	90.00	90.00	90.00	90.00	95.00	90.00	95.00	93.33	110.00	90.00	115.00
E3-med	90.00	90.00	90.00	90.00	95.00	100.00	100.00	98.33	115.00	100.00	115.00
E4-med	95.00	95.00	100.00	96.67	105.00	115.00	115.00	111.67	115.00	115.00	115.00
E5-med	105.00	100.00	95.00	100.00	115.00	115.00	100.00	110.00	115.00	115.00	115.00
E6-med	80.00	80.00	85.00	81.67	85.00	90.00	90.00	88.33	100.00	90.00	105.00
E7-med	95.00	95.00	95.00	95.00	105.00	100.00	95.00	100.00	105.00	105.00	115.00
E9-med	95.00	95.00	90.00	93.33	100.00	100.00	100.00	100.00	115.00	115.00	115.00
E10-med	80.00	75.00	75.00	76.67	90.00	85.00	75.00	83.33	95.00	95.00	115.00
E11-med	85.00	85.00	85.00	85.00	90.00	90.00	90.00	90.00	90.00	90.00	105.00
E12-med	100.00	100.00	105.00	101.67	95.00	115.00	105.00	105.00	115.00	115.00	115.00
E13-med	90.00	90.00	95.00	91.67	100.00	90.00	95.00	95.00	110.00	100.00	115.00
E14-med	85.00	80.00	90.00	85.00	105.00	100.00	95.00	100.00	110.00	110.00	115.00
E15-med	115.00	115.00	105.00	111.67	115.00	115.00	115.00	115.00	115.00	115.00	115.00
E16-med	95.00	90.00	95.00	93.33	115.00	115.00	100.00	110.00	115.00	115.00	115.00
E17-med	100.00	100.00	100.00	100.00	115.00	105.00	100.00	106.67	115.00	100.00	115.00
E18-med	100.00	95.00	95.00	96.67	105.00	100.00	100.00	101.67	110.00	100.00	115.00
E19-med	95.00	95.00	95.00	95.00	100.00	100.00	100.00	100.00	115.00	100.00	115.00
E1-unmed	90.00	85.00	100.00	91.67	100.00	95.00	95.00	96.67	115.00	115.00	115.00
E2-unmed	90.00	85.00	95.00	90.00	100.00	95.00	95.00	96.67	110.00	90.00	115.00
E3-unmed	95.00	90.00	90.00	91.67	95.00	100.00	100.00	98.33	115.00	115.00	115.00
E4-unmed	95.00	95.00	95.00	95.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00
E5-unmed	100.00	95.00	95.00	96.67	115.00	100.00	95.00	103.33	115.00	105.00	115.00
E6-unmed	85.00	80.00	85.00	83.33	90.00	95.00	90.00	91.67	115.00	95.00	100.00
E7-unmed	100.00	100.00	95.00	98.33	105.00	100.00	100.00	101.67	115.00	105.00	115.00
E9-unmed	100.00	95.00	100.00	98.33	105.00	105.00	100.00	103.33	115.00	115.00	115.00
E10-unmed	90.00	85.00	90.00	88.33	95.00	90.00	95.00	93.33			
E11-unmed	85.00	85.00	80.00	83.33	90.00	85.00	80.00	85.00	90.00	85.00	105.00
E12-unmed	90.00	85.00	85.00	86.67	100.00	90.00	90.00	93.33	85.00	105.00	115.00
E13-unmed	90.00	90.00	95.00	91.67	115.00	95.00	90.00	100.00	115.00	105.00	115.00
E14-unmed	85.00	85.00	90.00	86.67	105.00	95.00	95.00	98.33	110.00	110.00	115.00
E15-unmed	80.00	80.00	80.00	80.00	90.00	85.00	85.00	86.67	90.00	90.00	85.00
E16-unmed	95.00	85.00	90.00	90.00	105.00	100.00	95.00	100.00	115.00	105.00	105.00
E17-unmed	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00	115.00
E18-unmed	100.00	95.00	95.00	96.67	115.00	105.00	100.00	106.67	110.00	100.00	115.00
E19-unmed	90.00	90.00	85.00	88.33	115.00	100.00	100.00	105.00	115.00	100.00	115.00

APPENDIX D

AMPLITUDE RESOLUTION

Subject Number	Reversal Average
C1	3.50
C2	3.88
C3	3.80
C4	3.40
C5	2.50
C6	1.63
C7	1.00
C8	2.00
C9	2.60
C10	1.90
C11	3.50
C12	3.50
C13	0.80
C14	3.50
C15	3.00
C16	3.78
C17	3.09
E1- med	4.92
E2-med	2.50
E3-med	1.63
E4-med	2.05
E5-med	3.42
E6-med	0.25
E7-med	0.00
E9-med	1.64
E10-med	No Data
E11-med	5.62
E12-med	2.94
E13-med	1.70
E14-med	2.33
E15-med	3.91
E16-med	1.60
E17-med	1.77
E18-med	1.38
E19-med	3.50
E1-unmed	3.80
E2-unmed	0.75
E3-unmed	4.50
E4-unmed	No Data
E5-unmed	3.29
E6-unmed	No Data
E7-unmed	0.30
E9-unmed	0.86
E10-unmed	3.15
E11-unmed	6.20
E12-unmed	0.60
E13-unmed	9.50
E14-unmed	1.25
E15-unmed	3.15
E16-unmed	1.00
E17-unmed	2.14
E18-unmed	0.92
E19-unmed	0.40

APPENDIX E

BECK DEPRESSION INVENTORY-II

Subject Number	BDI-II
C1	6.00
C2	1.00
C3	0.00
C4	1.00
C5	0.00
C6	0.00
C7	0.00
C8	0.00
C9	0.00
C10	0.00
C11	0.00
C12	4.00
C13	2.00
C14	None
C15	3.00
C16	5.00
C17	1.00
E1-med	Refused
E2-med	14.00
E3-med	27.00
E4-med	6.00
E5-med	4.00
E6-med	13.00
E7-med	27.00
E9-med	11.00
E10-med	15.00
E11-med	19.00
E12-med	6.00
E13-med	5.00
E14-med	21.00
E15-med	2.00
E16-med	7.00
E17-med	8.00
E18-med	26.00
E19-med	29.00
E1-unmed	Refused
E2-unmed	35.00
E3-unmed	10.00
E4-unmed	29.00
E5-unmed	20.00
E6-unmed	3.00
E7-unmed	37.00
E9-unmed	2.00
E10-unmed	39.00
E11-unmed	18.00
E12-unmed	3.00
E13-unmed	4.00
E14-unmed	5.00
E15-unmed	5.00
E16-unmed	10.00
E17-unmed	5.00
E18-unmed	26.00
E19-unmed	8.00

APPENDIX F

AUDITORY BRAINSTEM RESPONSE

Subject Number	Lat 55SL-V	Amp 55SL-V
C1	5.22	1.21
C2	5.50	0.67
C3	5.76	1.34
C4	5.68	1.25
C5	5.70	1.20
C6	5.72	1.00
C7	5.74	0.75
C8	5.68	1.05
C9	5.76	0.83
C10	5.50	0.68
C11	5.72	1.21
C12	5.10	1.13
C13	5.76	0.82
C14	5.66	0.74
C15	6.04	0.77
C16	5.82	0.46
C17	6.06	0.89
E1- med	5.72	0.88
E2-med	5.78	0.81
E3-med	5.46	1.02
E4-med	5.39	1.08
E5-med	5.44	1.37
E6-med	5.52	0.98
E7-med	5.86	1.50
E9-med	5.72	1.28
E10-med	5.36	1.44
E11-med	5.76	1.01
E12-med	5.58	1.00
E13-med	5.54	0.66
E14-med	5.26	0.77
E15-med	5.94	1.41
E16-med	5.90	0.82
E17-med	5.88	0.87
E18-med	5.80	0.88
E19-med	5.64	0.73
E1-unmed	5.72	0.82
E2-unmed	5.80	1.02
E3-unmed	5.32	1.06
E4-unmed	5.90	1.03
E5-unmed	5.56	1.14
E6-unmed	5.64	1.21
E7-unmed	5.50	0.96
E9-unmed	5.74	1.05
E10-unmed	5.28	1.68
E11-unmed	5.74	0.95
E12-unmed	5.70	0.96
E13-unmed	5.40	1.27
E14-unmed	5.50	0.39
E15-unmed	5.84	1.45
E16-unmed	5.92	0.85
E17-unmed	5.98	0.75
E18-unmed	5.90	0.54
E19-unmed	5.60	0.84

APPENDIX G

AUDITORY LATE RESPONSE

Subject Number	ALR P1 55SL	ALR P1 45SL	ALR P1 35SL	ALR P1 25SL	ALR P1 15SL
C1	81.83	75.38	66.00		53.11
C2	64.52	71.86	81.24	71.86	63.66
C3	47.25	50.77	44.91	64.83	64.83
C4	69.52	68.35	74.21	70.69	83.58
C5	54.28	56.63	60.14	62.49	68.35
C6	64.83	66.00	70.69	67.18	62.49
C7	40.22	43.74	46.08	49.60	48.43
C8	54.29	56.63	63.66	63.66	81.24
C9	57.80	62.49	48.42	76.55	85.93
C10	36.70	41.39	46.08	44.91	48.43
C11	74.21	78.31	87.69	88.27	62.49
C12	42.56	43.74	42.56	58.97	53.11
C13	58.97	59.56	69.52	73.04	74.21
C14	59.56	61.32	60.14	69.52	61.32
C15	66.00	67.18	58.97	74.12	66.00
C16	47.25		63.66	64.83	
C17	66.00	64.83	71.86	80.07	71.86
E1- med	39.64	46.08	71.86	68.35	70.69
E2-med	66.59	68.94	71.28	67.18	69.52
E3-med	71.28	71.86	63.66	67.18	69.52
E4-med	64.25	61.32	61.32	63.66	53.11
E5-med	57.21	56.63	51.94	54.87	48.42
E6-med	61.32	53.44	55.46	62.49	67.18
E7-med	81.83	82.41	87.10	74.21	89.44
E9-med	44.91	50.77	73.04	69.52	91.79
E10-med	63.66	60.73	58.98	61.94	61.91
E11-med	55.46	54.28	58.97	53.11	68.35
E12-med	73.04	67.18	90.62	68.35	58.97
E13-med	60.73	60.14	48.42	56.63	53.11
E14-med	58.97	62.49	62.49	63.66	67.18
E15-med	68.94	63.66	77.72	73.04	47.84
E16-med	57.87	42.56	47.25	40.22	63.66
E17-med	58.97	64.25	44.91	50.77	49.60
E18-med	70.69	69.52	69.52	75.38	77.72
E19-med	67.18	64.83	68.35	67.18	71.86
E1-unmed	40.22	41.39	54.28	58.97	62.49
E2-unmed	63.42	67.18	64.83	61.32	58.97
E3-unmed	58.66	60.14	58.97	74.21	70.69
E4-unmed	63.51	69.52	69.52	60.14	34.36
E5-unmed	40.22	50.77	50.77	58.97	53.11
E6-unmed	57.38	55.46	64.84	66.00	70.70
E7-unmed	72.45	70.69	66.00	67.18	85.93
E9-unmed	46.67	56.63	66.00	69.52	49.01
E10-unmed	53.08	63.66	63.08	57.80	63.66
E11-unmed	53.11	55.46	46.08	51.94	51.94
E12-unmed	63.66	92.96	75.38	69.52	99.99
E13-unmed	66.00	61.32	67.18	66.00	75.38
E14-unmed	43.74	50.77	47.25	56.63	49.60
E15-unmed	47.25	34.36	56.63	82.41	
E16-unmed	45.50	46.08	50.77	56.63	42.56
E17-unmed	39.64	44.91	55.46	49.60	56.63
E18-unmed	47.25	47.25	51.94		56.63
E19-unmed	68.35	67.77	64.83	62.49	59.56

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